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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/753,851	12/02/96	WEINBERG J	1579-21

EXAMINER

HM11/1001

GAMBEL, P

ART UNIT	PAPER NUMBER
1644	46

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DATE MAILED: 10/01/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 12/2/96; 6/24/97; 7/22/98; 9/23/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 8-12, 14-19, 21-25 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 8-12, 14-19, 21-25 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40517

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Group 1640, Technology Center 1600.

2. Applicant's Status Inquiry, filed 7/22/98 (Paper No. 45) is acknowledged. This Office Action should serve in response to said inquiry.

3. The text of those sections of Title 35 USC not included in this Action can be found in prior Actions. The rejections of record can be found in previous Office Actions (Paper No. 16/22/34/38/41).

4. Applicant's amendment, filed 12/2/96 (Paper No. 43), is acknowledged.

Applicant's amendment, filed 6/24/97 (Paper No. 44), is acknowledged.
Claims 21-24 are added.

Applicant's amendment, filed 9/23/98 (Paper No. 45), is acknowledged.
Claim 25 was added.

It is noted that claim 25 was added to replace previously unentered claim 20.

Claims 1-7 and 13 have been canceled previously.
Claim 20 was not entered.
Claims 8-12 and 14-19 and 21-25 are pending.

Upon consideration that the instant claims are free of the prior art, this Office Action will be considering both previously elected and nonelected species encompassing anti-CD44 antibodies, soluble CD44, CD44 oligopeptides and hyaluronate

Therefore, claims 8-12, 14-19 and 21-25 are under consideration.

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 26.
Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes.

6. Claims 21 and 22 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "a compound, different from said agent, that blocks receptors for HIV infection on said cells" or "a compound, different from said anti-CD44 antibody, that blocks receptors for HIV infection on said mononuclear phagocyte"

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention and that the invention, in that context, is whatever is now claimed.. See MPEP 2163.02. Also, the failure to meet the written description requirement under 35 USC 112, first paragraph arises when the claims are changed after the filing date to change the scope of the disclosure, which does encompass setting forth subgeneric claims (see MPEP 2163.05).

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Here, the instant application has been held deficient under 35 USC 112, first paragraph, because the written description in the specification as filed is not adequate to identify what the appellant now claims or has invented.

The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action
Alternatively, applicant is invited to provide clear written support for the newly added "limitations" set forth above.

7. Claims 8-12 and 14-19 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has not disclosed how to use CD44-specific antibodies, soluble CD44, CD44 oligopeptides and hyaluronate to inhibit HIV infection or to inhibit CD44-facilitated HIV infection therapeutically in humans. There is insufficient information or nexus of the invention with respect to the in vitro or in vivo operability of claimed therapeutic strategies to inhibit HIV infection or to inhibit CD44-facilitated entry of HIV into cells in vivo or into monocytic cells in vitro in a mixed cell population.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of biopharmaceutical drugs such as antibodies can be species- and model-dependent, it is not clear that reliance on the in vitro inhibition of monocyte infection by a particular HIV strain (Example on page 31 of the instant specification) accurately reflects the relative efficacy of the claimed therapeutic strategies, which broadly encompass preventing or treating HIV infection, as disclosed in the specification and commensurate in scope with the claimed invention.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

It is noted that the instant specification relies upon the observation that the present invention provides a new method based on a separate molecular pathways of blocking HIV infection, that is, the CD44 receptor (hyaluronate receptor) facilitates HIV infection/expression in human cells, particularly mononuclear phagocytic cells. Further, it is noted that under certain defined in vitro conditions in a single working example, HIV infection and expression of normal human monocytes with certain HIV strains can be inhibited to a certain degree with anti-CD44 antibodies and hyaluronic acid in vitro only.

The claimed methods utilizing CD44-specific agents comprising CD44-specific antibodies/peptides and hyaluronic acid/hyaluronate appears limited to monocytic cells (versus lymphocytes) and does not completely inhibit infection of one HIV isolate in these cells under defined culture conditions. Therefore, it is not clear how the CD44-specific agents could inhibit HIV infection by various HIV strains in mixed leukocyte populations either in vitro or in vivo.

It is noted that both the examiner and the applicant have agreed that the instant application has demonstrated the ability of CD44-specific antibodies to inhibit HIV infection of mononuclear phagocytes in vitro under defined conditions. However, the examiner and the applicant have disagreed whether this would be predictive of the ability of CD44-specific antibodies to inhibit HIV infection of any susceptible cell in vitro and in vivo. The rejection of record has not been based upon an issue of 100% effectiveness, as argued by applicant. It is noted that applicant asserts the skilled artisan would appreciated that in vivo and ex vivo treatments would be appropriate. Also, applicant asserts CD44-specific antibodies would be appropriate in the prevention of any susceptible host cell including blood.

In the absence of objective evidence commensurate in scope with the claimed methods, applicant has not provided convincing objective evidence that the claimed invention is effective as a therapeutic or preventative for HIV infection based on the in vitro inhibition of HIV infection of monocytes in vitro alone.

With respect to the newly added claimed limitations comprising the use of reverse transcriptase inhibitors (claims 21-22); it is clear that the instant specification is relying upon the combination of CD44-specific agents and not just the role of reverse transcriptase inhibitors to treat HIV infection, as encompassed by the claimed invention. For example, page 30 of the instant specification discloses that the claimed CD44-specific agents can be used alone or in combination with alternative forms of HIV therapy to decrease the number of HIV-infected cells or to decrease the spread of virus from cell to cell or to lessen the infectability of HIV in products for infusion into humans to prevent HIV infection or the spread of HIV infection. Therefore, the instant rejection is based upon the unpredictability of CD44-specific agents on treating mixed cells populations in vitro and in vivo, rather than the role of reverse transcriptase inhibitors per se.

It has been well known in the art that retroviral infections in general, and HIV infections, in particular, have been refractory to anti-viral therapies. Further, it has been well known in the art that individuals infected with HIV produce neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion. Further, as disclosed by Fahey et al. (Clin. Exp. Immunol., 1992; of record), clinical trials monoclonal antibodies therapies have not provided any clinical benefits and "it is not clear how adding these additional antibodies would make a difference (see page 3, column 2, paragraph 3). Similarly, Hirsch et al. (N. Eng. J. Med., 1993; of record) clearly teach that the success of translating promising avenues of investigation into clinical practice has been meager (Page 1806, column 1, paragraph 2). For example, while soluble CD4 is a potent inhibitor of finding of certain strains of HIV-1 to CD4 cells in vitro, clinical HIV-1 isolates are less susceptible to such inhibition (page 1691, column 1, paragraph 2). Therefore, the art does recognize the benefit of even HIV-specific or CD4-specific (versus claimed CD44-specific) inhibitors can block HIV infection clinically.

Furthermore, it is noted that Rivaderneira et al. teach CD44-specific antibodies could inhibit the monocytotropic HIV-1-BaL infectivity of monocytic cells to some degree under certain culture conditions but could not block lymphocytotropic HIV-1 infection (manuscript filed with the 12/23/93 amendment, Paper No. 18). Guo et al. also teach anti-CD44 antibodies did not inhibit infection (J. Immunol., 1993; see entire document, particularly page 2234, column 2, paragraph 1; of record).

Dukes et al. (J. Virol., 1995) similarly discloses that anti-CD44 antibodies can inhibit productive HIV-1 infection of mononuclear phagocytes in vitro, but not lymphocytes (see entire document). The Discussion acknowledges that membrane compounds may be required for HIV-1 binding, entry and productive infection, CD4 function as the predominant membrane receptor for HIV-1. Therefore, the in vivo therapeutic methods do not address this major target of HIV infection nor the breadth of cell types with receptors for HIV infection.

Pearce-Pratt et al. (Biology of Reproduction, 1996) also discloses the limitations of in vitro models on the in vivo transmission of HIV and that in 1996, further research was still required (see entire document, particularly Introduction and Discussion).

Also, it is noted that while there may some evidence that CD44-specific agents including CD44-specific antibodies/peptides and hyaluronic acid/hyaluronate can inhibit HIV infection and expression under in vitro conditions; there is insufficient evidence that the mechanism of action operates via CD4-facilitated entry of HIV into cells. For example, Ueno et al. (U.S. Patent No. 4,840,941) discloses the criticality of sulfate groups in the inhibition of HIV infectivity and reverse transcriptase activity (see entire document, particularly Example 9).

It has been well known in the art that cellular CD4 has been recognized as the predominant membrane protein that interacts with HIV. However, it has been well known that HIV infection occurs in cells that express variable or no detectable levels of CD4. It has been well known that $CD4^+$ T cells are the primary target of HIV infection both in vitro and in vivo. Therefore, it would not have been predictable that targeting CD44 in mononuclear phagocytes would affect HIV infection of any susceptible cell either in vitro or in vivo. For example, either the individual or the blood would be infected by HIV via CD4, irregardless of blocking CD44 infectivity of mononuclear phagocytes. Further, it is noted that CD44-specific antibodies can block HIV infection of mononuclear phagocytes in vitro, however these same antibodies can not block the infection of mitogen-stimulated lymphocytes or cells of a T lymphocyte line in vitro (Rivadeneira et al., Aids Research and Human Retroviruses, 1995; see entire document including Abstract; of record). Therefore applicant's assertions of record have not appeared consistent with applicant's own observations.

Appellant's assertions of record have run contrary to current understanding of the lack of predictability of HIV treatments as well as that at the time the invention was made as acknowledged in Ex parte Balzarini 21 USPQ2d 1892 (1991), which stated that skilled persons and the evidence of record supports the conclusion that in vitro testing of anti-viral compounds is not in and of itself predictive of in vivo efficacy in the treatment of retroviral diseases broadly or specifically AIDS (page 1896, column 2, paragraph 2).

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective HIV-specific/adhesion-based/antibody-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting HIV infection in vivo or to all cells. It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification alone.

Applicant's arguments of record have not been found persuasive and the rejection is maintained. It is noted that if applicant limits claims to the in vitro inhibition of HIV infection of mononuclear phagocytes or monocytes, then the rejection under 35 U.S.C. § 112, first paragraph would be withdrawn. It is noted that claims 19 is drawn to the in vitro inhibition of CD44-facilitated HIV infection of mononuclear phagocytes in vitro, however the claims read on a mixed cell population and not a phagocytic population alone.

8. Claims 8-12 and 14-19 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A) Claims 8-12 and 14-19 and 21-25: With respect to the open language "comprising" and the scope of the claims reading on reverse transcriptase inhibitors as recited in claims 21-22; the following is noted.

There is insufficient direction and guidance to reverse transcriptase inhibitors other than "zidovudine" on page 30 of the instant specification. It is noted that the incorporation of zidovudine triphosphate into an elongating nucleic acid by reverse transcriptase and its competitive inhibition of thymidine-5'-triphosphate appears to be the primary mechanism of anti-HIV action of this drug. However, the instant specification does not provide an appropriate mechanism of action of reverse transcriptase inhibitors, which can encompass a number of mechanisms of actions or guidance and does not provide guidance as to other reverse transcriptase inhibitors that may be appropriate at the time the invention was made. The scope of the claims must bear a reasonable correlation with the scope of enablement. Without such guidance, making and using reverse transcriptase inhibitors to treat HIV infection and expression commensurate in scope with the claimed methods is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

It is noted that "zidovudine" may be a trademark or trade name. Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark or the trade name "zidovudine" is used to identify or describe a reverse transcriptase inhibitor, and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

B) Claims 8 and 21:

With respect to agents that inhibit CD44-facilitated entry of HIV into cells sufficient to effect said inhibition other than CD44-specific antibodies/peptides and hyaluronic acid/hyaluronate; there is insufficient guidance and direction to agents commensurate with the enablement provided by the disclosure with regard to the large number of putative "agents" broadly encompassed by the claims. Further, the claims broadly encompass a significant number of inoperative species. It is not sufficient to define a specificity by its principal biological activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed "agents" in manner reasonably correlated with the scope of the claims broadly including any number of "agents". Also, it is noted that minor structural differences even among structurally related compounds or compositions can result in substantially different pharmacological activities. The scope of the claims must bear a reasonable correlation with the scope of enablement. Without such guidance, the changes which can be made in the agent's structure and still maintain HIV inhibitory activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

9. Claims 21-22 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "compounds, different from said anti-CD44 antibody, that blocks receptors for HIV infection on said mononuclear phagocyte" because the characteristics of the "compounds" are not known and ill-defined. This language is vague and indefinite since it encompasses potentially thousands of different "compounds" and it is not apparent from the disclosure which particular "compounds" are being referred to. These "compounds" could be any molecule, with no apparent function or practical use, as well as known and unknown. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "compounds" encompassed by the claimed invention. The recitation of "compounds" fails to distinctly claim what that protein is and what the compositions are made up of. Therefore, there is insufficient information and guidance for the metes and bounds of the nucleic acids encoding said "compounds, different from said anti-CD44 antibody, that blocks receptors for HIV infection on said mononuclear phagocyte".

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of such "compounds, different from said anti-CD44 antibody, that blocks receptors for HIV infection on said mononuclear phagocyte" nor is there sufficient evidence provided that such "compounds" could be used in a practical manner either in vitro or in vivo. It would require undue experimentation to produce all such possible "compounds" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "different compounds". It is readily apparent from the claimed invention what is the scope of "compounds", targeted "receptors" as well as the direct/indirect mechanisms of action of blocking HIV receptors encompassed by the claimed invention. Applicant has failed to enable or provide written description for the myriad of "compounds" and fails to provide any guidance to those skilled generally on how to make and use useful "compounds that differ from anti-CD44 antibodies. While the specification discloses soluble CD44, CD44 oligopeptides and hyaluronate; reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods which rely upon "compounds diffferenfr om said anti-CD44 antibodies" commensurate in scope with the claimed invention using the teaching of the specification alone.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

10. Claim 11: It is apparent that the A1G3 antibody/hybridoma is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specifciaiton. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a depost of the hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

It is noted that the ATCC Catalog (8th Edition, 1994) discloses that the A1G3 (ATCC HB-177) antibody/hybridoma is available under the conditions that you will not use it for commercial purposes or distribute it to third parties. Therefore, the claimed antibody does not appear to be publicly available.

Biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a given depository prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the depository, nor is there any evidence as to the depository's policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the AG13 antibody/hybridoma is readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

It is noted that requirement under 35 USC 112, first paragraph for the A3D8 antibody has been satisfied by its public/commercial availability, as evidenced by its availability from Sigma Chemical Company (see Catalog 1995, page 1171).

11. Claims 10-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 10 is indefinite in the recitation of the peptides in the absence of the recitation of the appropriate SEQ ID NOS. Applicant is required to amend the claims to recite the appropriate SEQ ID Nos. to clearly define the metes and bounds of the claimed peptides.

B) Claim 11 is indefinite in the recitation of "A1G3" because their characteristics are not known. The use of "A1G3" monoclonal antibodies as the sole means of identifying the claimed antibodies renders the claim indefinite because these terms are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas.

C) The amendments must be supported by the specification so as not to add any new matter.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

14. Claim 8, 9, 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ueno et al. (U.S. Patent No. 4,840,941). Ueno et al. Teach the use of hyaluronic acid and salts and pharmaceutical compositions thereof to treat HIV infection. Although this reference is silent about the CD44-facilitated entry of HIV infection and it is not clear that the mechanism of action by which hyaluronic acid/hyaluronate inhibit HIV infection is via CD44-mediated entry; this reference does teach the use of hyaluronic acid to inhibit retroviral and HIV infection (see entire document, particularly column 2, line 52; column 5, paragraph 2, Example 9). Given applicant's assertion that hyaluronic acid/hyaluronate inhibit HIV via the CD44-mediated pathway, it appears that the referenced teaching of inhibiting HIV infection with hyaluronic acid would operate via this mechanism as well. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the claimed methods would be inherent properties of the referenced hyaluronic acid/hyaluronate. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

15. Claims 8, 9 ,12 and 22 are rejected under 35 U.S.C. § 103 as being unpatentable over Ueno et al. (U.S. Patent No. 4,840,941) in view of the art known use of AZT (zivodudine) to treat HIV infections at the time the invention was made.

Ueno et al. Is taught above in section 14, which teaches the use of hyaluronic acid/hyaluronate in the treatment of HIV infections. It is noted that Ueno et al. Does not use the term "hyaluronate" per se but this pharmaceutical formulation would have known and readily apparent to the ordinary artisan at the time the invention was made, given the referenced teaching. This reference is silent about the use of reverse transcriptase inhibitors per se, even though it uses the reverse transcriptase assay. The use of AZT at the was known and used by the ordinary artisan at the time the invention was made to treat HIV infection.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

One of ordinary skill in the art at the time the invention was made would have been motivated to select the combination of hyaluronic acid/hyaluronate and reverse transcriptase inhibitor such as AZT to inhibit HIV infection under a number of in vitro, ex vivo and in vivo regimens. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. It is noted that applicant has clearly stated that the instant invention is not drawn to the use of CD44-specific immunotoxins and that the current claimed recitation supports this conclusion.

17. No claim is allowed.

It is noted that claims drawn to methods of inhibiting HIV infection of mononuclear phagocytes (versus a mixed cell population) in vitro with CD44-specific antibodies would be considered allowable.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
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Group 1640
Technology Center 1600
October 1, 1998